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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,346	04/15/2005	Stefan Frahling	GIL-16027	8225

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EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,346	FRAHLING ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,10,15-20 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,10,15-20 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

STATUS OF APPLICATION

Applicants' Amendments and Remarks filed on 29 April 2010, in the matter of Application N° 10/531,346, are acknowledged and entered on the record. The Examiner further acknowledges the following:

No claims have been amended or canceled.

Claims 24-27 are newly added. Applicants allege support for claim 24 where the instant disclosure discusses "enhanced solubility" (pg. 17) and the components comprising the freeze-dried article, namely the preferred alginates (pg. 7). The limitations of claim 24 are further discussed herein (see **NEW REJECTIONS**).

Support for the newly added property limitations of the skeleton-forming agent in claims 25-27 is provided by Applicants (pg. 7, lines 3-27).

Claims 1, 4-6, 10, 15-20 and 23-27 now represent all claims currently under consideration.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statements (IDS) have been filed for consideration.

NEW OBJECTIONS/REJECTIONS

In light of Applicants' newly added claims, namely claim 24, the following rejection is added:

CLAIM REJECTIONS - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Dependent claim 24 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Newly added claim 24, recites a limitation to the method of claim 1 such that the shaped article which is produced is not cross-linked. Applicants' response, dated 29 April 2010, alleges two passages in the disclosure as representing support for the amendment. The first citation is to page 7, lines 7-9, which discusses calcium-free sodium alginate (e.g. most preferably less than 1.5 wt%) as being a preferred low-viscosity skeleton-forming agent of the composition. The second citation is to page 17, lines 23-32, which discusses the rates of dissolution of the article as measured in accordance with a particular method and apparatus according to *PharmEU*. The Examiner respectfully submits that after carefully examining both of the above passages in their entirety, support for the newly added limitation with respect to the scope of the invention is lacking. The Examiner understands Applicants' reasoning for the amendment is to preferably exclude forms of sodium alginate which comprise higher amounts of calcium as calcium ions exhibit cross-linking within alginates. However, the scope of the limitation as presently recited is not commensurate with the support provided; the claim recites that the composition is completely free of cross-linking. Applicants' support is thus not supportive of other means for accomplishing cross-linking (i.e.

cross-linking of starch compounds). Furthermore, the two above passages as presented in the disclosure, do not clearly or expressly relate the components (e.g. calcium-free sodium alginate) or the functional properties (e.g. enhanced dissolution) to the resulting property wherein the article is not cross-linked. Thus, the addition of the aforementioned limitation constitutes **new matter**, since Applicants' disclosure apparently lacks support for it. Herein and for the purposes of examination on the record, the new claim is broadly and reasonably interpreted in light of the remarks and passages provided by Applicants that a teaching in the art of calcium-free sodium alginate is indicative of an absence of cross-linking in the article formed in the invention of base claim 1 and new claim 24.

MAINTAINED REJECTIONS

The following rejections are maintained from the previous Office Correspondence dated 1 February 2010 since the art which was previously cited continues to read on the amended/newly cited limitations.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-6, 10, 15-20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Zecchino et al. (USPN 6,497,887) in view of Kojima et al.

The instant claim 1 is directed to a method of using a shaped article to apply at least one skeleton-forming agent to an external skin or hair surface of a human or animal comprising (1) providing a sized and shaped article, free of protein-based scaffolding agent, (2) disintegrate said article with an aqueous solution to form a solution or a gel, and (3) applying the composition to the intended surface. Said shaped article is further claimed as having a volume ranging from 100 microliters to 6 mL and a diameter ranging from 3-60 mm. The skeleton-forming agent recited in claim 1, is further recited as comprising at least one polysaccharide such as sodium alginate

(claims 4 and 5). Claim 6 recites the article as sphere-shaped prior to contact with water (claim 6). Claim 10 further limits the method at step (b) of claim 1 such that the aqueous solution which contacts the article (e.g. wetting solution) further comprises an active or auxiliary substance. Said substances are further delineated in claims 15 and 16, respectively. The shaped article is recited as further comprising one or more cosmetic or pharmaceutically active substances (claims 17 and 18) or one or more auxiliary substances such as squalane (claims 17-20). Claim 23, which depends from claim 10, further limits the article of claim 1 in the same manner as claim 17.

The invention of Zecchino anticipates the instantly claimed invention with the exception that Applicants' volumetric limitations are not expressly disclosed. The Abstract of Zecchino expressly discloses that the invention is directed to a delivery system for topical application to the skin comprising a freeze-dried membrane which can be reversibly returned to a dissolvable gel form upon the application of a wetting agent. Biologically active agents are released to the skin. Concerning the actual composition used by the instant method, Example 2 teaches a freeze-dried membrane (e.g. a shaped structure) which comprises both sodium alginate and squalane. The formulation is free of ingredients which are consistent with Applicants' definition of "protein-based skeleton forming agents" (i.e. enzymes, hormones, etc.) (see pg. 8, lines 5-9 of Applicants' specification). The limitations of claims 17-19 are also expressly taught by the formulation of Example 2. Potassium carbonate is well-known in the art as an alkalizing agent (i.e. a pH-adjusting agent). Rayon and hyaluronic acid are both well-known humectants; the former is also a plasticizer whereas the latter is also a lubricant. The cellulose gum is taught as a film-forming auxiliary substance (col. 3,lines 24-38). The limitations of claim 18 are met by Example 2 with the teaching of soluble collagen protein. "Soluble collagen", as defined by the art (see *Hawley's*

Condensed Chemical Dictionary, 13th Ed.), is a "fibrous protein constituting most of the white fiber in the connective tissues of animals and humans, especially in the skin muscles and tendons" (pg. 288, Hawley's). Nowhere is it indicated that soluble collagen is a "protein-based skeleton-forming agent", as defined by Applicants. Regarding the limitations of claims 10, 15 and 16, Zecchino teaches that in order to function on the skin, the prepared membrane must be rewetted with a wetting solution or activator (col. 3, line 57 to col. 4, line 13). It is further taught as being preferred that the applied wetting solution be slightly acidic (e.g. pH of 2-6) in order to facilitate dissolution of the matrix and that any aqueous solution containing a cosmetically or pharmaceutically acceptable acid will be appropriate for use in rewetting. Examples of different cosmetically or pharmaceutically acceptable acids such as malic acid are taught (col. 4, lines 6-13; Example 1).

Despite anticipating the chemical composition and method of application of the instant invention, the Zecchino reference is deficient in its teachings of both the volumetric limitations recited in step (a) of claim 1 and the geometrical sphere shape as recited in claim 6 by Applicants.

Regardless, a clear case of *prima facie* obviousness exists since the ordinarily skilled artisan would have been highly motivated to arrive at both the instantly claimed method and the composition used therein as evidenced by the express teachings discussed above.

Concerning the aforementioned deficiencies of Zecchino, since the volumetric ranges and geometric format of the article with respect to the claimed composition are adjustable, it follows that each is a parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. In the instant case, Zecchino expressly teaches in Example 1 that the

article produced is a lyophilized membrane wafers which are sliced to a thickness of 0.5 mm. Formation of any desired freeze-dried shape is also expressly taught and suggested (col. 3, lines 39-55). Though the specific shape of a sphere is not taught, the formation of wettable objects is any shape is well known in the art, as evidenced by the previous teachings (e.g. Figure 6F) of Kojima et al. (US Pre-Grant Publication N° 2002/0068683). Thus, it would have been customary for an artisan of ordinary skill, to adjust the size and shape of in the composition used by the method, particularly in view of the forgoing teachings, in order to achieve the desired composition and method. See also MPEP §§2144.04(IV)(A.) and 2144.05. Thus, absent some demonstration of unexpected results or criticality from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

RESPONSE TO ARGUMENTS

Applicants' arguments with regard to the rejection of claims 1, 4-6, 10, 15-20 and 23 under 35 USC 103(a) as being unpatentable over the combined teachings of Zecchino et al. and Kojima et al. have been fully considered but they are not persuasive.

Applicants' response, namely the fourth paragraph on page five of the Remarks and the bridging paragraph of pages five and six appear to traverse the Examiner's use of Example 2 of Zecchino as a teaching of the composition used in the instant invention. It is admittedly unclear to what passage in Zecchino Applicants are referring (see first line of bridging paragraph, page 5). The first full paragraph on page six of the Remarks more clearly traverses the rejection on the grounds that any presence of collagen is regarded as a cross-linking agent. Applicants provide evidence of this definition pointing to their own disclosure (e.g. pg. 1, lines 24-30), *Hawley's*

Condensed Chemical Dictionary, and USPN 4,795,467. Applicants lastly allude to a process known as dehydrothermal treatment or DHT, which is stated as a process wherein collagen is cross-linked by simultaneously subjecting collagen to high heat and freeze-drying in order to facilitate cross-linking.

In response, the Examiner respectfully disagrees and submits that Applicants' evidence is not commensurate in scope with the present invention or the art which is applied (e.g. Zecchino et al.). It appears from the response provided by Applicants that they are moving to establish that *any* presence of collagen within a composition such as those taught by Zecchino necessitates the presence of cross-linking properties. The Examiner has carefully considered all of the evidence provided.

Concerning the definition set forth in Applicants' disclosure (e.g., pg. 1, lines 24-30), the Examiner notes that the definition on which Applicants rely is founded in the three German patent documents which are mentioned at the beginning of the paragraph, the English equivalents of which are USPNs: 5,387,415; 5,384,129; 5,401,502; and 5,405,616. The Examiner considers these teachings to be indicative of the state of the art regarding the ability of collagen to act as a cross-linking agent. However, in each of the formulations discussed by these references, collagen is used in amounts which exceed 50% w/w. Despite discussing freeze-drying as part of their processes, it is respectfully pointed out that these references fail provide a definition which helps in overcoming the Zecchino reference of record. The references discussed by Applicants, which allegedly speak to the cross-linking properties of collagen, do so in the context whereby collagen represents at least half of the freeze-dried composition or more. The Zecchino reference employs soluble collagen as 1% of its formulations in Examples 1 and 2.

Concerning Applicants' mentioning of the *Hawley's* definition of "soluble collagen", the Examiner notes that the definition also says that "soluble collagen" becomes increasingly cross-linked with age. There is no evidence within the Zecchino reference which would suggest to the ordinarily skilled artisan that the formulations are prepared using dated or aged material. Furthermore, the definition provided by *Hawley's* is broadly and reasonably interpreted as stating that soluble collagen *may* become cross-linked as it ages [emphasis added].

Turning to Applicants' mentioning of the '467 reference, the Examiner notes this an example of such conditions which may be applied to collagen as means for facilitating and exploiting its cross-linking properties. The reference to this patent is respectfully considered as being immaterial to both the instantly claimed invention as well as the applied Zecchino reference, particularly since neither discusses the application of heat in any manner, let alone in relation to cross-linking of collagen.

Lastly, concerning Applicants remarks to the term "dehydrothermal cross-linking", the Examiner respectfully admits it was not immediately possible to find a clear definition or teaching in the art of a process in which *any* substance, let alone collagen, is simultaneously subjected to heat treatment and freeze-drying in order to achieve a cross-linking effect [emphasis added]. It is respectfully requested that if Applicants are aware of any such teachings that they be made of record. Based on what Applicants have stated on the record concerning "dehydrothermal crosslinking", the Examiner notes that such a process, again, necessarily involves heating the collagen component in order to achieve cross-linking. As discussed above, heating the composition is not commensurate in scope with either the instant invention or the art of record.

It is understood based on the Remarks provided that Applicants ultimately seek to overcome the Zecchino reference by arguing that the referenced compositions contain soluble collagen and therefore necessarily contain "a protein-based skeleton-forming agent".

The Examiner respectfully disagrees with this position for the following reasons.

First, the Zecchino reference, particularly the aforementioned Example 2, forms a freeze-dried gel membrane whose predominant component is a polymer which has the potential to become crosslinked (e.g. crosslinkable polymer) (claim 1). Said polymer may be selected from alginates, collagen and starches (claim 2). The Example expressly uses sodium alginate in an amount of 48 wt% of the composition (i.e. the most abundant of the formulation).

Second, the Examiner recognizes, as would the ordinarily skilled artisan, that the Zecchino reference employs soluble collagen in the Examples in a very small amount (e.g. 1 wt%). Otherwise stated, it is recognized that collagen, in these instances, is not being relied upon for its ability to possibly become crosslinked. To add further clarification to this interpretation, Zecchino is interpreted as teaching two different forms of collagen for two different purposes. Clearly, as discussed above, Zecchino sets forth that "collagen", as a functional alternative to alginates, may be employed as the predominant polymer of the gel membrane (e.g., claim 2). As the primary constituent of the gel membrane, the ordinarily skilled artisan would reasonably expect that collagen, in this role, would be more likely to exhibit crosslinking properties. Set apart from this is Zecchino's teaching of "soluble collagen" as a second form of collagen which may be employed in a miniscule amount as an active substance (see col. 5, lines 28-34; Example 2).

Turning to Applicants' aforementioned comments, namely of the fourth paragraph on page five of the Remarks and the bridging paragraph of pages five and six, the Examiner notes that

Applicants look to clarify the passage of the instant disclosure at page 8, lines 5-9. Specifically, Applicants admit on the record that "[t]he cited paragraph ... does not refer to the definition of protein-based skeleton forming agents but instead to protein-based *active substances*, which are *explicitly not excluded* from the invention by use of the phrase "skeleton-forming agents, proteins being excepted"". The Examiner in considering this definition of an active substance provided by Applicants, broadly and reasonably interprets the scope of the claim to include those protein-based compounds which are employed as active substances. The definition provided by Applicants does not specifically exclude collagen. Rather the definition is interpreted as being open-ended and inclusive of any such protein-based active ingredient. Applicants affirm this interpretation on the record in their acknowledgement that protein-based active substances are explicitly, not excluded from the invention (i.e. which is to say, they are included).

Given Applicants' discussion concerning which type of compounds are eligible for use in the composition as active ingredients, it stands to reason that a clear showing in the art of a protein-based compound employed as an active agent would read on the instant invention. Zecchino, as discussed above, not only provides such a teaching, but also sets apart one form of collagen and its use from another form/use, in terms of function and amount.

For these reasons, Applicants' arguments while having been carefully considered, are found unpersuasive. Said rejection is therefore **maintained** and extended to include newly added claims 24-27. The limitation of claim 24 is discussed above and is interpreted, based on the alleged support, as not only adding new matter, but also as being directed to a method of using a composition formed using calcium-free sodium alginate. Claims 25-27 are interpreted as being directed to the same limitations particularly since the properties recited therein are the same as

those offered as the alleged support for claim 24. The properties are interpreted in light of the instant disclosure as being directed towards calcium-free sodium alginate.

The Zecchino reference is considered by the Examiner as reading on these limitations, for two reasons. First, the reference clearly sets apart calcium and sodium alginate embodiments of the gel membrane polymer. Second, Example 2 employs 48 wt% of sodium alginate. At no point is it indicated that calcium is in any way a part of this composition. Thus, the composition of Example 2 is interpreted as being silent to any amount of calcium (e.g. 0 wt% calcium).

All claims have been rejected; no claims are allowed.

CONCLUSION

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615